120

01/28/04

A RCE

1636

PTO/SB/30 (05-03)
Approved for use through 04/30/2003. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

REQUEST FOR CONTINUED EXAMINATION (RCE) TRANSMITTAL

Address to: RCE
Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Application Number	**09/721,543**
Filing Date	**November 21, 2000**
First Named Inventor	**LIU, FENYONG**
Art Unit	**1636**
Examiner Name	**NGUYEN, QUANG**
Attorney Docket Number	**BERK-005**

This is a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114 of the above-identified application.
Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. See Instruction Sheet for RCEs (not to be submitted to the USPTO) on page 2.

1. Submission required under 37 C.F.R. § 1.114
   - a. ☒ Previously submitted
     - i ☒ Consider the amendment(s)/reply under 37 C.F.R. § 1.116 previously filed on **June 25, 2003-copy attached**
       (Any unentered amendment(s) referred to above will be entered).
     - ii ☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____
     - iii ☐ Other _____
   - b. ☐ Enclosed
     - i ☐ Amendment/Reply
     - ii ☐ Affidavit(s)/Declaration(s)
     - iii. ☐ Information Disclosure Statement (IDS)
     - iv. ☐ Other _____

2. Miscellaneous
   - a. ☐ Suspension of action on the above-identified application is requested under 37 C.F.R. § 1.103(c) for a period of _____ months. (Period of suspension shall not exceed 3 months; Fee under 37 C.F.R. § 1.17(i) required)
   - b. ☐ Other _____

3. Fees The RCE fee under 37 C.F.R. § 1.17 (e) is required by 37 C.F.R. § 1.114 when RCE is filed.
   - a. ☒ The Director is hereby authorized to charge the following fees, or credit any overpayments, to Deposit Account No. **50-0815**
     - i ☒ RCE fee required under 37 C.F.R. § 1.17 (e)
     - ii ☒ Extension of time fee (37 C.F.R. §§ 1.136 and 1.17)
     - iii ☒ Other **Fee Transmittal, Copy of Advisory Action, Postcard**
   - b. ☐ Check in the amount of $ _____ enclosed
   - c. ☐ Payment by credit card (Form PTO-2038 enclosed)

     WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

Name (Print/Type)	**Pamela J. Sherwood**	*Registration No. (Attorney/Agent)*	**36,677**
Signature	Pamela Sherwood	*Date*	January 26, 2004

EXPRESS MAIL LABEL NO. EV333998083US

01/30/2004 MAHMED1 00000001 500815 09721543

01 FC:2801 385.00 DA

PTO/SB/17 (10-03)
Approved for use through 07/31/2006. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

FEE TRANSMITTAL for FY 2004

Effective 10/01/2003. Patent fees are subject to annual revision.

☒ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 1390

Complete if Known	
Application Number	09/721,543
Filing Date	November 21, 2000
First Named Inventor	LIU, FENYONG
Examiner Name	NGUYEN, QUANG
Art Unit	1636
Attorney Docket No.	BERK-005

METHOD OF PAYMENT (check all that apply)

☐ Check ☐ Credit Card ☐ Money Order ☐ Other ☐ None

☒ Deposit Account:

Deposit Account Number: 50-0815

Deposit Account Name: Bozicevic, Field & Francis LLP

The Director is authorized to: (*check all that apply*)

☒ Charge fee(s) indicated below ☒ Credit any overpayments

☒ Charge Any Additional Fee(s) Required under 37 C.F.R. 1.17.

☐ Charge fee(s) indicated below, **except for the filing fee to the above-identified deposit account.**

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	770	2001	385	Utility filing fee	
1002	340	2002	170	Design filing fee	
1003	530	2003	265	Plant filing fee	
1004	770	2004	385	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	
				SUBTOTAL (1)	

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

	Extra Claims		Fee from below		Fee Paid
Total Claims	-20**	=	x	=	
Indep. Claims	-3**	=	x	=	
Multiple Dependent				=	

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	86	2201	43	Independent claims in excess of 3
1203	290	2203	145	Multiple dependent claim, if not paid
1204	86	2204	43	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) $

***or number previously paid, if greater; For Reissues, see above.*

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge – late filing fee or oath	
1052	50	2052	25	Surcharge – late provisional filing fee or cover sheet	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examination action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	420	2252	210	Extension for reply within second month	
1253	950	2253	475	Extension for reply within third month	
1254	1,480	2254	740	Extension for reply within fourth month	
1255	2,010	2255	1,005	Extension for reply within fifth month	1,005
1401	330	2401	165	Notice of Appeal	
1402	330	2402	165	Filing a brief in support of an appeal	
1403	290	2403	145	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive – unavoidable	
1453	1,330	2453	665	Petition to revive – unintentional	
1501	1,330	2501	665	Utility issue fee (or reissue)	
1502	480	2502	240	Design issue fee	
1503	640	2503	320	Plant issue fee	
1406	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	770	2809	385	Filing a submission after final rejection (37 CFR § 1.129(a))	
1810	770	2810	385	For each additional invention to be examined (37 CFR § 1.129(b))	
1801	770	2801	385	Request for Continued Examination (RCE)	385
1802	900	1802	900	Request for expedited examination of a design application	
				Other fee (specify) _____	

*Reduced by Basic Filing Fee Paid **SUBTOTAL (3) ($)** 1390

SUBMITTED BY				Complete (*if applicable*)	
Name (Print/Type)	Pamela J. Sherwood	Registration No. (Attorney/Agent)	38,677	Telephone	(650) 833-7790
Signature	Pamela Sherwood			Date	01/26/2004

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www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/721,543	11/21/2000	Fenyong Liu	BERK-005	2657

24353 7590 07/21/2003

BOZICEVIC, FIELD & FRANCIS LLP
200 MIDDLEFIELD RD
SUITE 200
MENLO PARK, CA 94025

EXAMINER
NGUYEN, QUANG

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 07/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

SMP RS

07/25/03
Appeal Brief 08/25/03
LD 01/25/04

Advisory Action

Application No.	Applicant(s)
09/721,543	LIU ET AL.
Examiner	**Art Unit**
Quang Nguyen, Ph.D.	1636

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

THE REPLY FILED 15 June 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on *25 June 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1,6,8,10,12-16,19,21,23,25 and 26*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

DAVID GUZO
PRIMARY EXAMINER

Continuation of 2. NOTE: The newly amended claims 6, 12-14, 16, 15, 16, 19, 23 and 25-26 raise a new ground of rejection, specifically under 35 U.S.C. 112, second paragraph. For example, the lack of antecedent basis for the limitations "said RNA" in the proposed claim 6, "composition" in proposed claims 12-14, "said polynucleotide" in the proposed claim 15, and "said antiviral polynucleotide" in the proposed claim 16. Additionally, the scope of the amended claims 6 and 8 is not the same as the scope of the finally rejected claims. This is because the polynucleotide ligand in the proposed claims 6 and 8 is not required to possess an anti-hCMV activity.

Continuation of 5. does NOT place the application in condition for allowance because: Applicants' arguments are not found to be persuasive for the reasons discussed below and that these have been discussed more extensively in the Final Office Action.

(1) With respect to the Written Description rejection, Applicants argue that a representative number of species has been provided, and that three separate examples of sequences (L13, L19 and L66) have demonstrated anti-viral activity. Additionally, specific examples of polynucleotide ligands meeting the requirements of the claims are provided in Tables 1 and 2.

Please note that apart from the sole disclosure of the L19 ligand having SEQ ID NO:12 and the ability to block hCMV entry into targeted cell via its specific binding to hCMV envelope glycoprotein gB in the elected group of RNA polynucleotide ligand sequences, the instant specification fails to disclose a representative number of RNA polynucleotide ligands that have hCMV antiviral activity via the binding of any hCMV envelope or capsid proteins, particularly for a broad genus of elected RNA polynucleotide ligands of from 15 to 100 nucleotides in length that share sequence similarity or common core structure to any of SEQ ID NOs:12-16. Additionally, apart from the common functional limitation of binding to a hCMV and inhibiting hCMV infection, the specification fails to disclose or identify the relevant structural characteristics or common essential core elements that are responsible for the desired functions, not even for the L19 ligand, let alone for any other RNA ligands of from 15 to 100 nucleotides in length. What are the sequences (necessary for a proper 3-dimensional folding or by other means) that these RNA ligands need to possess in order for them to exhibit an anti-hCMV activity? It is also noted that there is no direct correlation between the ability of an RNA polynucleotide ligand that binds to hCMC and its ability to block hCMV entry into a cell as evidenced by the teachings of the present application for the ligands L17 and L31 (see examples 1 and 2 of the instant specification). Furthermore, adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it, and that the Written description provision is severable from its Enablement provision.

(2) With respect to the scope of Enablement rejection, Applicants argue that the sequences of SEQ ID NO:12-16 meet the requirements of 35 U.S.C. 112 as evidenced by the statements "In our study, the selected ligands exhibited a high affinity to hCMV particles and were highly effective in inhibiting viral production" and "the binding affinity of the ligands also appeared to correlate with their activity in inhibiting viral infection". Applicants further argue that the ligands cited by Examiner that lack antiviral activity are unrelated to the presently claimed invention because the presently claimed sequences share specific sequence motifs, e.g., the terminal TGGG sequence, and the internal motif purine-CCC(AT/TA) as well as other similarities, and therefore these sequences should also have antiviral activity.

Please note the cited statement "the binding affinity of the ligands also APPEARED to correlate with their activity in inhibiting viral infection". Additionally, there is no objective evidence of record indicating or suggesting that the sequence motifs: TGGG sequence, the internal motif purine-CCC(AT/TA) are essential for the binding of the L19 ligand to the hCMV glycoprotein gB that blocks effectively hCMV entry into targeted cells. Although the ligands L17 and L31 do not fall within the elected group of RNA polynucleotide ligand sequences, they demonstrate that simply binding to hCMV does not necessarily lead to the inhibition of hCMV entry into targeted cells. This supports the Examiner's position that the anti-hCMV activity has to be detemined empirically, and that there is no way to predict which nucleotide modification (addition, deletion, substitution) at which nucleotide position and in which combinations to the ligand L19 having SEQ ID NO:12 would or would not result in the RNA polyncleotide ligand variants possessing the desired anti-hCMV activity. Furthermore, the courts have stated that reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in the patent application.